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# CLAIMS AS AMENDED DURING INTERNATIONAL PRELIMINARY EXAMINATION

<SEE RESPONSE TO FIRST WRITTEN OPINION FILED February 22, 2005 WITH IPEA/EP>

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This is in response to the Written Opinion issued on 22 December 2004 in the above case. An extension of 1 month was requested and granted, cf. our telephone conversation with Mr. Delmon on 1 February 2005 and the subsequent issuance of IPEA 427 dated 10 February 2005.

Applicant has previously notified the International Preliminary Examining Authority (IPEA) that Applicant can accept a late issued IPER.

Applicant would like to have resolved in the international phase of the above application the issues of novelty and inventive step relating to the following claims:

amended claim 1 (based on orignal claim 1 and page 33, lines 13-15, and page 83, lines 21-22),
amended claim 32 (based on original claim 44),
amended claim 43 (based on original claim 59),
amended claim 49 (based on original claim 65),
amended claim 53 (based on original claims 69 and 94),
amended claim 79 (based on original claim 96 and page 8, lines 3-4),
amended claim 83 (based on original claim 99),
amended claim 85 (based on original claim 101),
amended claim 86 (based on original claim 102), and
amended claim 93 (based on original claim 111 and page 26, lines 6-7 and 16-23).

Also, Applicant desires to obtain from the IPEA an acknowledgement that the above-mentioned group of claims is directed to a group of inventions having a single, general inventive concept, i.e. the novel and inventive, beaded polymer matrix now cited in claim 1.

Should the IPEA reach the conclusion that issues preventing issuance of a favourable International Preliminary Examination Report in respect of novelty, inventive step and unity of invention have not been dealt with in the enclosed response, issuance of a Second Written Opinion is hereby requested.

A telephone interview with the IPEA is requested in accordance with PCT Rule 66.6 in the event that the IPEA is unable to issue a Second Written Opinion.

Applicant would like to retain the possibility of attending - at the discretion of the IPEA - a personal interview with the IPEA in the event the IPEA is unable to issue a favourable International Preliminary Examination Report in the present case.

Claim amendments – relationship between original claims and presently amended claims

Claim 1 is amended as detailed herein below.

Claims 2-6 are unchanged and correspond to original claims 2-6.

Original claims 7 and 8 are deleted.

New claims 7 and 8 cite from 4 to 10 and from 4 to 8 microparticles, respectively. Basis can be found e.g. on page 32, lines 26 to 28, and page 33, lines 13 to 15.

Claims 9-31 correspond to original claims 11-33. Claim dependencies have been amended accordingly.

Original claims 34-43 are deleted.

Claims 32-37 correspond to original claims 44-49. Claim dependencies have been amended accordingly.

Original claims 50 to 53 are deleted.

Claims 38-42 correspond to original claims 54-58. Claims dependencies have been amended accordingly.

Claims 43-77 correspond to original claims 59-93. Claim dependencies have been amended accordingly. Claim 53 is amended to cite a method for distance matrix determination (previously cited in original claim 94, now deleted).

Claim 78 corresponds to original claim 95. Claim dependency has been amended accordingly.

Claims 79-81 correspond to original claims 96-98. Claim dependencies have been amended accordingly. Claim 79 is now directed to geometrical figures in the form of triangles and quadrangles. The basis for this amendment can be found e.g. on page 8, lines 3-4.

New claim 82 is based on original claim 96 and page 8, lines 3-4.

Claims 83-102 correspond to original claims 99-119 with the exception that original claims 108 and 109 have been deleted. Claim dependencies have been amended accordingly. Claim 93 is amended to cite vi) a computer running a program for calculation of distance matrices, and the limitation to the CCD-cameras and the gated image intensifiers and the optical objective which is now cited in the last part of the claim.

Unity of Invention

Unitary groups I and II as defined by the ISA have been searched. These groups relate to

original claims 1-68 (Group I); and

original claims 69-98, 100 (partly), and 111-119 (Group II).

Group I as defined by the ISA now contains the following independent claims as amended:

Claim 1 relating to a beaded polymer matrix comprising a plurality of microparticles.

Claim 32 relating to a composition comprising a plurality of different beads according to any of claims 1 to 31.

Claim 43 relating to a method for the detection of spatial positions of microparticles in a composition of beads according to any of claims 32 to 42.

Claim 49 relating to a method for generating the polymer matrix according to any of claims 1 to 31.

Group II as defined by the ISA now contains the following independent claims:

Claim 53 relating to a method for distance matrix determination of spatially encoded microparticles in the polymer matrix according to any of claims 1 to 31.

Claim 79 relating to a method for identifying individual beads in the composition of different beads according to any of claims 32 to 44, said method employing the method of any of claims 53 to 78 for the determination of a distance matrix.

Claim 93 relating to a device for recording and storing the image of an encoded bead.

Applicant does not agree with the above groupings in view of the introduced amendments to claim 1.

As the claims have now been amended,

as claim 1 is directed to novel and inventive subject matter as argued herein below, and

as at least the following claims:

amended claim 1,
amended claim 32,
amended claim 43,
amended claim 49,
amended claim 53,
amended claim 79,
amended claim 83,
amended claim 85,
amended claim 86,
amended claim 93,

are joined by a single, general inventive concept in the form of the spatially encoded, novel and inventive bead according to claim 1 (or a composition of such different, spatially encoded beads

according to claim 32), there is no justification for upholding the division into four distinct, unitary groups of inventions.

Claim 83 is directed to a method for identifying a spatially encoded bead of the composition of any of claims 32 to 42. There is no justification for not acknowledging the unity which exists between the method of claim 83 and e.g. the methods of any of claims 53 and 79.

Claim 85 is directed to a method for recording individual reaction steps performed on a spatially encoded bead of the composition of any of claims 32 to 42. There is no justification for not acknowledging the unity which exists between the method of claim 85 and e.g. the methods of any of claims 53 and 79.

Claim 86 is directed to a method for identifying a chemical compound and employs the recording method of claim 85.

Accordingly, Applicant requests that amended claims 53, 79, 83, 85 and 86 be rejoined with the remaining groups of inventions belonging to Group I, the reason for the request being that all said claims are all linked by a general inventive concept.

The single, general inventive concept of all of the above-mentioned claims is furthermore supported by W13/89 stating that the principle set out in the case law relating to the old version of Rule 13.2 PCT (corresponding to the old version of Rule 30 EPC) remains unchanged.

In the old version of Rule 13 PCT, the combinations of

a product (i.e. present claims 1 and 32),
a process adapted for the manufacture of the product (i.e. present claim 49), and
a use of the product (i.e. present claims 43, 53, 79, 83, 85, and 86)

were held to be unitary.

The above and well established principle for unitary groups of inventions should also apply to the present case.

**Invention I as defined by the ISA**

Amendment to claim 1

In Applicants opinion, novelty of

claim 1 (beaded polymer matrix) will confer novelty on

claim 32 (composition of different (novel) beads according to claim 1),
claim 43 (method employing the (novel) composition according to claim 44),
claim 49 (method for generating the (novel) beaded polymer matrix according to claim 1),
claim 53 (method for distance matrix determination of (novel) bead according to claim 1),
claim 79 (method for identifying (novel) beads in (novel) composition according to claim 44),
claim 83 (method for identifying (novel) beads in (novel) composition according to claim 44),
claim 85 (method for recording reaction steps performed on (novel) bead according to claim 1),
claim 86 (method for identifying chemical compound based on recording steps of claim 85).

Also, claims depending on the above-mentioned claims will be novel provided that claim 1 is novel.

Claim 1 is amended to cite:

"An encoded beaded or granulated polymer matrix comprising a plurality of spatially immobilised particles or vacuoles, wherein each particle or vacuole is individually detectable, wherein the encoded bead has a diameter of from 0.5 millimeter to less than 2.0 millimeter and comprises from 3 to 10 microparticles."

The amendment to the above claim 1 is based on original claim 1, page 33, lines 13 to 15, and, indirectly, on the bead diameter values stated in claim 91 as published with the Pamphlet.

As the lower end point of the above diameter range is explicitly stated in claim 91 and forms part of the larger, general range of from 0.1 millimeter to less than 2.0 millimeter, it is submitted that the amendment does not contravene the requirement of Art 34(2)(b) PCT. Reference is made to T 925/88 in view of, among others, T2/81 (CLBA (4th. Ed.), p. 220).

Novelty

Claim 1 as amended is novel over D1.

D1 and amended claim 1 of the present application disclose distinct ranges of microbead densities, i.e. number of microbeads per bead volume.

D1 discloses on page 8 synthesis particles of a diameter of from 100-300 µm preferably containing from 5 to 25 dispersed microparticles. In contrast, the present invention as cited in claim 1 relates to a beaded polymer matrix having a diameter of from 500 to 2000 µm and containing from 3 to 10 dispersed microparticles.

The larger size of the beads and the relatively small number of microparticles distinguish the encoded polymer matrix according to the present invention from a beaded synthesis particle according to D1 having a smaller size and a comparatively higher number of microparticles. Differences between the beads according to the invention and the beads according to D1 are summarized in the below table.

| Property | Unit | Symbol | D1 | | Carlsberg | |
|---|---|---|---|---|---|---|
| | | | min | max | min | max |
| bead diameter | micrometer | D | 100 | 300 | 500 | 2000 |
| bead volume | microliter | V | 0,0005 | 0,0141 | 0,0654 | 4,1867 |
| projected bead area | square millimeter | A | 0,0079 | 0,0707 | 0,1963 | 3,1400 |
| number of microbeads | | N | 5 | 25 | 3 | 10 |
| microbead density* | microbeads per microliter | N/V | 354 | 47771 | 1 | 153 |
| projected microbead density** | microbeads per square millimeter | N/A | 71 | 3185 | 1 | 51 |

* The maximum microbead density is calculated by dividing the maximum number of microbeads with the minimum bead volume. The minimum microbead density is calculated by dividing the minimum number of microbeads with the maximum bead volume.

** The maximum projected microbead density is calculated by dividing the maximum number of microbeads with the minimum projected bead area. The minimum projected microbead density is calculated by dividing the minimum number of microbeads with the maximum projected bead area.

The volume, V, of a spherical bead is given by:

$$V = 4/3 \cdot \pi \cdot R^3$$

where R = D/2 is the radius of the bead, and D is the diameter of the bead.

It follows that

$$V = 4/3 \cdot \pi \cdot (D/2)^3$$

The projected bead area, A, of a spherical bead is equal to the central cross-sectional area of the bead and is given by

$$A = \pi \cdot R^2 = \pi \cdot (D/2)^2$$

The microbead density, N/V, is given by the number of microbeads, N, divided by the bead volume, V.

The projected microbead density, N/A, is given by the number of microbeads, N, divided by the bead volume, A.

As an example, consider a 100 micrometer (0,1 mm) diameter bead with 25 microbeads as disclosed in D1. The volume is given by,

$$V = 4/3 \cdot \pi \cdot (0{,}1/2)^3 \text{ mm}^3 = 0{,}0005 \text{ mm}^3 = 0{,}00052 \text{ microliters}$$

The projected bead area is given by

$$A = \pi \cdot (0{,}1/2)^2 \text{ mm}^2 = 0{,}0079 \text{ mm}^2$$

Accordingly, the preferred maximum microbead density is given by the highest number of microparticles in the smallest possible volume, i.e.

$$N/V = 25/0{,}00052 = 47771 \text{ microbeads/microliter}$$

which is the preferred maximum microbead characterising the beaded synthesis particles according to D1.

Similarly, the preferred maximum projected microbead density is given by

$$N/A = 25/0{,}0079 = 3185 \text{ microbeads/mm}^2$$

which is the preferred maximum projected microbead density characterising the beaded synthesis particles according to D1.

A minimum microbead density of 354 microbeads per microliter is calculated for beaded synthesis particles according to D1 having a diameter of 300 micrometer (0,3 mm) diameter and containing 5 microbeads. The corresponding projected microbead density is 71.

In summary, it can be seen from the above table that whereas the beaded synthesis particles according to D1 have a microbead density (microbeads per microliter) of from 354 to 47771, the microbead density of the encoded polymer beads according to the present invention (as defined in claim 1) is from 1 to 153 microbeads per microliter.

Accordingly, the beads have different microbead densities and can thus clearly be distinguished from each other.

As the microbead density of an encoded bead according to the present invention is different from the microbead density of an encoded bead according to D1, novelty of an encoded, beaded polymer matrix according to the present invention over the beaded synthesis particles disclosed in D1 should be acknowledged.

Claim 1 as amended is novel over D3

D3 discloses two methods for encoding beads. Both of said methods result in beads having different physical properties than the encoded beads defined by claim 1 as amended.

The first encoding method disclosed in D3 (Method I) is a method resulting in fluorescent silica colloids being attached to the outer surface of a bead (see Fig. 2a and 2b). The beads are 0.1 millimeter in diameter, i.e. outside the range claimed in amended claim 1.

Another difference between Method I of D3 and the present invention is that the microparticles of the present invention are embedded in a bead and not attached to the outer surface of a bead.

Method II of D3 is concerned with a different principle of encoding and discloses a bead having concentric layers of "optical signatures". This is different from the discrete microparticles used in the present invention.

Nowhere does D3 disclose beads having from 3 to 10 spatially immobilised microparticles dispersed in said beads.

Accordingly, the novelty of amended claim 1 over D3 should be acknowledged.

Claim 1 as amended is novel over D4

D4 discloses in claim 1 and 2 a structure comprising a core and one or more layers disposed around said core. This principle is different from the discrete microparticles embedded within a bead used in the present invention.

D4 discloses in claim 13 a structure comprising a substrate having a plurality of areas on the surface each of which can emit light of different wavelengths. Again, this principle is different from the discrete microparticles embedded within a bead used in the present invention.

Nowhere does D4 disclose beads having from 3 to 10 spatially immobilised microparticles dispersed in said beads.

Accordingly, the novelty of amended claim 1 over D4 should be acknowledged.

Claim 1 as amended is novel over D5

D5 discloses a structure comprising, among others, a doped semiconductor nanocrystal electromagnetic radiation emitting and amplifying phase and a high index of refraction contrast electromagnetic radiation scattering phase. Such a material is fundamentally different from a beaded polymer comprising a plurality of microparticles.

Nowhere does D5 disclose beads having from 3 to 10 spatially immobilised microparticles dispersed in said beads.

Accordingly, the novelty of amended claim 1 over D5 should be acknowledged.

Claim 1 as amended is novel over D6

The Written Opinion states in section 1.2 under "Invention I" that D6 teaches the subject matter of claim 65. Applicant disagrees and kindly requests the Examiner to point out to Applicant the section of the document which the Examiner has in mind - this is not clear from the general reference to D6 in the above section of the Written Opinion.

Novelty can only be destroyed by citing features of a prior art document, not by making a vague reference to the general content of a prior art reference. Nowhere does D6 disclose beads having from 3 to 10 spatially immobilised microparticles dispersed in said beads.

Accordingly, the novelty of amended claim 1 over D6 should be acknowledged.

Conclusion - Novelty of Invention I as defined by the ISA

Section 1.2 under "Invention I" in the Written Opinion states that the present invention lacks novelty over D1, D3, D4, D5 and D6.

Applicant has demonstrated herein above that amended claim 1 is novel over each and all of D1, D3, D4, D5 and D6.

As claim 1 relating to a beaded polymer matrix is novel, the novelty of

claim 32 (composition of different (novel) beads according to claim 1),
claim 43 (method employing the (novel) composition according to claim 44),
claim 49 (method for generating the (novel) beaded polymer matrix according to claim 1),
claim 53 (method for distance matrix determination of (novel) bead according to claim 1),
claim 79 (method for identifying (novel) beads in (novel) composition according to claim 44),
claim 83 (method for identifying (novel) beads in (novel) composition according to claim 44),
claim 85 (method for recording reaction steps performed on (novel) bead according to claim 1),
claim 86 (method for identifying chemical compound based on recording steps of claim 85),

as well as claims depending on the above-mentioned claims, should also be acknowledged.

Inventive step

The closest prior art is D1.

The present invention has shown that encoded beads comprising from 1 to up to about 150 microbeads per microliter can be identified in the methods for encoded bead identification disclosed in the present application.

Practical measurements of spatially immobilised microbeads dispersed in polymer beads also revealed that it is often difficult to readily identify beads having a microbead density of more than about 300 microbeads per microliter.

Accordingly, encoded beads, such as the ones disclosed in D1, having more than about 350 microbeads per microliter cannot readily be identified in a composition of different beads each having a high microbead density of more than about 350 microbeads per microliter.

The difficulty of identifying encoded beads having a high microbead density - i.e. more than about 350 microbeads per microliter - is due to the fact that the probability of encountering what is known as "correspondence problems" increases with an increasing microbead density.

The correspondence problem can broadly be described as the problem of distinguishing two different encoded beads from each other. Correspondence problems will arise when the three-dimensional (3D) positions of microbeads inside an encoded bead are to be determined based on two or more images (projections) of the encoded bead recorded from different angles. In short, a correspondence problem arises when two or more encoded beads harbouring spatially immobilised microparticles cannot be unambiguously identified from images of the spatially immobilised microbeads obtained from different angles.

The correspondence problem is illustrated in Fig. 10 and an experimental evaluation of the significance of the problem is presented on pages 23-25 in the present application. It is clear that the number of beads having a correspondence problem correlates positively with an increased number of microparticles per bead, i.e. an increased microbead density.

Accordingly, it will be increasingly difficult to overcome and solve a correspondence problem when the number of spatially immobilised microbeads is increased from e.g. 10 to e.g. 25. This can be seen e.g. from the simulation disclosed in the top part of Fig. 11 illustrating the number of spatially encoded beads with a "correspondence problem". The simulation experiment is described in more detail on pages 23-25 in the description.

In contrast to the low microbead density of from 1 to about 150 microbeads per microliter employed with the spatially encoded beads according to the present invention, D1 discloses encoded beads having a high microbead density, i.e. a microbead density of from about 350 to about 48.000 microbeads per microliter (see page 8, lines 24-26 of D1).

The technical problem to be solved can be formulated e.g. as how to achieve a better identification, or a more simple or easy identification, of a spatially encoded bead, c.f. page 5, lines 27-30, of the description of the present application.

In order to overcome the above stated technical problem one can - in principle - either

a) invent a more sensitive method which aims to overcome one or more of the problems stated in the state of the art, and/or

b) invent spatially encoded beads which are more readily identifiable than state of the art encoded beads using state of the art identification methods.

The present application - in relation to a) above - discloses on pages 21 and 22 of the description three approaches which can be used to increase the sensitivity of a state of the art method for encoded bead identification.

Furthermore, in relation to b) above, claim 1 is directed to a low microbead density encoded bead which clearly differs from the state of the art encoded beads disclosed in D1.

The bead diameter of the beads of D1 is preferably from 100 to 300 micrometers (see page 8, lines 24-25 in D1). Other bead diameters can also be used, c.f. page 6, lines 14-16, of D1. Importantly, nowhere in D1 - apart from page 8, lines 24-26 - can the skilled person obtain any guidance as to the relationship between bead diameter and microparticle number. Accordingly, the skilled person is unable to evaluate whether the microbead density should be increased, or decreased, or remain the same, when the bead diameter is changed.

Based on the figures of D1 it is clear that the number of macroparticles can even be increased to numbers well above the preferred range of from 5 to 25 stated on page 8, lines 24-26. In fact, figure 1 illustrates a white bar of about 35 millimeters in length just above the text "X350 100 µm". X350 is thus most likely the magnification of the image.

On the balance of probabilities, and as there is no other reference in the text of D1 to the diameter of the bead of figure 1, the skilled person would most likely infer from the text in the figure "X350 100 µm" that a distance of 35 millimeters (i.e. length of white bar on the figure) corresponds to a bead diameter of 100 µm (35 millimeters / 350 (degree of magnification) = 0.10 millimeter = 100 µm). 100 µm matches exactly the citation of this number in the figure next to the degree of magnification.

Accordingly, as the diameter of the bead in figure 1 of D1 is about 75 millimeters (measured using an ordinary ruler), the diameter of the bead is likely to be about 75 / 35 millimeters x 100 µm = 214 µm. This bead diameter is well within the preferred diameter range stated on page 8, lines 24-26, i.e. a diameter range of from 100 µm to 300 µm. However, the number of microparticles (white dots in figure 1) far exceeds the maximum preferred number of 25 stated in D1 on page 8, lines 24 to 26. Consequently, D1 is in fact guiding the skilled person towards a seemingly alternative solution which not only points away from the preferred solution (5 to 25 microparticles), but also results in a significantly increased microparticle density - the exact opposite solution as the one being suggested in the present application.

Although the image of the bead presented in figure 2 is of a lesser contrast than the image of the bead presented in figure 1, it is never-the-less possible to roughly estimate the bead diameter in the same way as is done herein above for the bead in figure 1. It is submitted that the diameter of the bead of figure 2 is about 75 millimeters / 5 millimeters x 10 µm = 150 µm. Again, the bead diameter is within the preferred interval, but the number of microparticles would appear to exceed the preferred maximum of 25. Accordingly, figure 2 of D1 also seems to point the skilled person in another direction - i.e. towards a significantly increased microbead density - as compared to the much different direction suggested by the present invention: Larger bead size and fewer microparticles - the result being a much lower microbead density.

Apart from the above differences in microbead densities, the microparticles illustrated in figures 1 and 2 of D1 clearly suggests that it is possible to perform a distance matrix determination for microparticles which are scattered on the surface of the bead in a random pattern "like a constellation of stars" (c.f. D1, page 7, lines 23-24). Accordingly, it is somewhat unclear how the term "distance matrix determination" as used in D1 should be interpreted in view of this apparent possibility. Applicant is of the opinion that the term "distance matrix determination" does not

necessarily have the same meaning in all embodiments of the invention disclosed in D1 as the meaning attached to "distance matrix determination" in the present application.

Furthermore, D1 discloses only hydrophobic polymers as bead materials. This choice of polymer material would potentially disable use of the beads in aqueous media, and this would appear to limit use of the beads for applications that require aqueous conditions, e.g. a wide range of biological assays.

The present invention discloses both hydrophobic polymers as well as hydrophilic polymers to be used as bead materials. This choice would enable the use of aqueous media for suspension of the beads, and this would enable the use of the beads for applications for which the beads disclosed in D1 are not suitable.

In summary, the inventive step associated with claim 1 should be acknowledged. Nowhere can the skilled person find any guidance for the solution proposed by the present invention: Spatially encoded beads having a larger size and a lower microbead density. The preferred spatially encoded beads of D1 have a higher microbead density and D1 alone or in combination with any of the other documents identified in the International Search Report do/does not motivate the skilled person to make the choice of increasing the bead size <u>and</u> lowering the microbead density.

In fact, the figures of D1 which - according to page 9, lines 14-15, of D1 - illustrate the alleged invention disclosed in D1 even seems to suggest that an equally feasible solution would be to increase even further the microparticle density from the already significantly high density of about 350 microparticles per microliter (c.f. the above table).

The composition according to claim 32 is inventive as it comprises a plurality of different, novel and inventive encoded beads according to claim 1.

The method of claim 43 is inventive as it relates to a method for detecting spatial positions of microparticles in the novel and inventive composition according to claim 44 (c.f. C-IV,9.12).

The method of claim 49 is inventive as it relates to a method for generating the novel and inventive, beaded polymer matrix according to claim 1 (c.f. C-IV,9.12).

**<u>Invention II as defined by the ISA</u>**

<u>Amendment to claim 53 (original claim 69)</u>

Claim 53 is amended by incorporating the subject matter of original claim 94 into present claim 53. This is believed to overcome the rejection raised by the Examiner in section 1.1. under "Invention II" in the Written Opinion.

Accordingly, amended claim 53 now cites - in addition to the original wording of claim 69 - the method steps of original claim 94 directed to distance matrix determination.

As a consequence of the amendment to claim 53, original claim 94 is deleted and the remaining claims are renumbered.

<u>Amendment to claim 79 (original claim 96)</u>

Claim 79 is amended by citing geometrical figures selected from triangles and quadrangles. Basis for the amendment can be found e.g. on page 8, lines 3-4.

## Amendment to claim 93 (original claim 111)

Amended claim 93 now cites - in addition to the original wording of original claim 111 - the feature of a computer running a program for calculation of distance matrices for individually spatially encoded beads, as well as the further features of "gated image intensifiers" of CCD camera, "optical focussing objective" of said gated image intensifiers, and "fluorescence filter" og said optical objective.

## Novelty

### Claim 53 as amended is novel over D1

Claim 53 as amended is novel as the claim is directed to a method for distance matrix determination of the novel and inventive encoded bead according to claim 1 and claims depending on claim 1. The novelty resides in the provision in step i) of the novel and inventive polymer matrix according to claim 1.

### Claim 79 as amended is novel over D1

Claim 79 as amended is novel as the claim is directed to a method for distance matrix determination of the novel and inventive encoded bead according to claim 1 and claims depending on claim 1. The novelty resides in the recording of geometrical figures in the form of triangles or quadrangles.

### Claim 93 as amended is novel over D2

D2 discloses a general apparatus for imaging and analysing parameters of - in particular - biological cells. Nowhere does D2 disclose a computer running a program for calculation of distance matrices for individually spatially encoded beads.

### Conclusion - Novelty of Invention II

The novelty of amended claim 53 is conferred by the provision to the method of a novel (and inventive) spatially encoded bead according to claim 1 (c.f. step i) of the method of claim 53).

The novelty of claim 79 is conferred by the novelty of the method of claim 53 (c.f. step i) of the method of claim 53), as well as by the geometrical figures selected from triangles and quadrangles.

The device according to amended claim 93 is novel over D1 and D2 as neither D1 nor D2 disclose the combination of features cited in amended claim 93, including the feature vi) a computer running a program for calculation of distance matrices for individual, spatially encoded beads.

## Inventive step

Claims 53 and 79 are inventive as they relate to a method for distance matrix determination and identification, respectively, of the novel and inventive, spatially encoded bead according to claim 1 (c.f. C-IV,9.12).

D2 is the closest prior art to amended claim 93. Amended claim 93 is associated with an inventive step over D2 as D2 does not disclose or motivate the skilled person to combine features i) to vi) to arrive at the claimed invention.

Acknowledgement of receipt

We thank the European Patent Office for acknowledging safe receipt of this letter by means of the enclosed EPO Form 1037.

Yours sincerely
HØIBERG A/S

Jesper Levin Aamand

Amended set of claims (1-102)
EPO Form 1037